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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/892,505 | 06/28/2001 | Saluh Kivlighn | 50193-109 | 4997 |

7590 02/05/2007

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| EXAMINER | |
|---|---|
| KANTAMNENI, SHOBHA | |
| ART UNIT | PAPER NUMBER |
| 1617 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 02/05/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/892,505 | KIVLIGHN ET AL. | |
| | Examiner | Art Unit | |
| | Shobha Kantamneni | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *None* is/are allowed.

6)☒ Claim(s) *16-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This office action is in response to the communication filed on 11/21/2006.

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/08/2006 has been entered.

Applicant's amendment filed on 11/21/2006, wherein new claims 16-17 have been added, and claims 1, 5, 7, and 14 have been canceled.

In view of the newly added claims, and new ground(s) of rejections, the rejections made in the final office action are herein withdrawn.

Currently, claims 16-17 are pending.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's amendment with respect to new claims 16-17 has been fully considered but is deemed to insert new matter into the claims since the specification as originally filed does not provide support for the limitation, "effective amount of a composition comprising a xanthine oxidase inhibitor, or a pharmaceutically acceptable salt thereof, to achieve a uric acid level in the patient of 4 to 6 mg/dl". The original specification merely discloses that uric acid levels of >4 and <6 mg/dl in a patient are at reduced risk of cardiovascular conditions such as hypertension, coronary heart disease, renal dysfunction, cardiovascular morbility and mortality. See page 11, lines 20-31. The specification as originally filed does have support for reducing uric acid comprising administering a "therapeutically effective amounts of a composition comprising a xanthine oxidase inhibitor to achieve a uric acid level of >4 and <6 mg/dl".

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "therapeutically effective amount of a composition comprising a xanthine oxidase inhibitor or a pharmaceutically acceptable salt thereof to achieve a

uric acid level in the patient of 4 to 6 mg/dl" in claims 16-17 is indefinite, as it is not clear what this term encompasses, the specification does not clearly define this term, and one of ordinary skill in the art could not ascertain the metes and bounds as to "therapeutically effective amount xanthine oxidase inhibitor" to achieve a uric acid level in the patient of 4 to 6 mg/dl.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Maeda et al. (5,747,495, PTO-892), in view of Ward (Lancet 1988, 352, pages 670-671, PTO-892).

Maeda et al. discloses a method of treating hypertension comprising administering to a patient in need thereof a therapeutically effective amount of a uric acid lowering agent, a xanthine oxidase inhibitor, 4-amino-6-hydroxypyrazolol [3,4-d]pyrimidine (AHPP). See abstract; column 2, lines 11-13; column 6, Example 9, claim 1. For oral administration of AHPP, the effective antihypertensive amount is 100-9000 mg/day/adult patient. See column 2, lines 63-65. It is also taught that uric acid

production was inhibited by AHPP in a dose dependant manner. See column 4, Example 5.

Maeda et al. do not explicitly teach the administration of a therapeutically effective amount of xanthine oxidase inhibitor to achieve a uric acid level in the patient of 4 to 6 mg/dl in treating hypertension.

Ward teaches that uric acid is a risk factor for hypertension associated morbidity and mortality. See page 670, left hand column bottom paragraph-right hand column, line 9. It is also taught that hypertensive people with serum uric acid levels of 5.0-6.9 mg/dL had a significantly higher risk for both heart attack, and stroke.

It would have been obvious to a person of ordinary skill in the art to determine the optimal parameters such effective amounts of xanthine oxidase inhibitor needed to achieve desired results i.e uric acid level in the patient of 4 to 6 mg/dl, because 1) Maeda et al. teaches that uric acid production was inhibited by xanthine oxidase inhibitor, AHPP in a dose dependent manner, and 2) the optimization of amounts of known agents to be administered to achieve a desired effect, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. One of ordinary skill in the art at the time of invention would have been motivated to optimize the amount of xanthine oxidase inhibitor with reasonable expectation of obtaining uric acid levels of 5.0-6.9 mg/dL in treating hypertension because Ward teaches that hypertension is associated with serum uric acid levels, and uric acid levels of 5.0-6.9 mg/dL had a significantly higher risk for both heart attack, and stroke.

Furthermore, it is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955.) Maeda et al. also exemplifies that uric acid production was inhibited by AHPP in a dose dependent manner.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Baldwin et al. (4,032,522, PTO-892), in view of Ward (Lancet 1988, 352, pages 670-671, PTO-892).

Baldwin et al. discloses a method of reducing uric acid in a patient by administering xanthine oxidase inhibitors, trifluoromethylimidazoles. See abstract; column 2. It is also disclosed that the compounds therein are anti-hyperuricemic agents, and exhibit anti-hypertensive activity. See column 5, lines 36-45; column 6, lines 5-52. The compounds therein are administered in an amount of 100-800 mg per day. See column 11, lines 50-54.

Baldwin et al. do not specifically teach the administration of a therapeutically effective amount of xanthine oxidase inhibitor to achieve a uric acid level in the patient of 4 to 6 mg/dl in treating hypertension.

Ward teaches that uric acid is a risk factor for hypertension associated morbidity and mortality. See page 670, left hand column bottom paragraph-right hand column, line 9. It is also taught that hypertensive people with serum uric acid levels of 5.0-6.9 mg/dL had a significantly higher risk for both heart attack, and stroke.

It would have been obvious to a person of ordinary skill in the art to determine the optimal parameters such effective amounts of xanthine oxidase inhibitor needed to achieve desired results i.e uric acid level in the patient of 4 to 6 mg/dl, since the optimization of amounts of known agents to be administered, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. One of ordinary skill in the art at the time of invention would have reasonably expected to treat hypertension by modifying the effective amounts of xanthine oxidase inhibitor to achieve desired uric acid levels because Ward teaches that hypertension is associated with serum uric acid levels.

Furthermore, it is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955.) Maeda et al. also exemplifies that uric acid production was inhibited by AHPP in a dose dependent manner.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16-17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamoto et al. (EP 0 337 350, PTO-1449), in view of Ward (Lancet 1988, 352, pages 670-671, PTO-892).

Nakamoto et al. discloses a method of lowering uric acid comprising administering a xanthine oxidase inhibitor, allopurinol. See page 2, lines 15-20. It is also disclosed that compounds that reduce uric acid are effective in curing hypertension. See page 6, lines 1-2.

Nakamoto et al. do not specifically teach the administration of a therapeutically effective amount of allopurinol to achieve a uric acid level in the patient of 4 to 6 mg/dl in treating hypertension.

Ward teaches that uric acid is a risk factor for hypertension associated morbidity and mortality. See page 670, left hand column bottom paragraph-right hand column, line 9. It is also taught that hypertensive people with serum uric acid levels of 5.0-6.9 mg/dL had a significantly higher risk for both heart attack, and stroke.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer allopurinol to treat hypertension.

One of ordinary skill in the art at the time of invention would have been motivated to administer allopurinol with reasonable expectation of success of treating hypertension by lowering uric acid because Nakamoto teaches that uric acid lowering agents are known to treat hypertension.

It would have been obvious to a person of ordinary skill in the art to determine the optimal parameters such effective amounts needed to achieve desired results i.e uric acid level in the patient of 4 to 6 mg/dl because Ward teaches that uric acid is a risk factor for hypertension, and uric acid levels of 5.0-6.9 mg/dL had a significantly higher risk for both heart attack, and stroke. Thus, one of ordinary skill in the art at the time of invention would have been motivated to optimize the effective amounts of allopurinol with reasonable success of lowering uric acid to desired levels to treat hypertension.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Tuesday, Thursday-Friday, 7.30 am-3.30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shobha Kantamneni, Ph.D
Patent Examiner
Art Unit : 1617

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER